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Effects of smoking on the cardiopulmonary modulation during physical exercise in middle-aged non-obese healthy individuals

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ABSTRACT

Aims: The aim of this study was to evaluate the overall effects of smoking and its duration on various cardiopulmonary modulation mechanisms during physical exercise in middle-aged non-obese healthy individuals.

Methods: Two hundred forty-three (142 smokers and 101 non-smokers), middle-aged, non-obese, healthy individuals were evaluated in this study. Parameters of pulmonary function including forced vital capacity (FVC), forced expiratory volume in the first second (FEV1) and FEV1/FVC ratio were evaluated using a spirometer and systolic pulmonary artery pressure (sPAP) were measured by echocardiography on rest and during various levels of exercise. A treadmill exercise test was used to assess heart rate recovery index (HRRI), the chronotropic index (CI) and the maximum rate of oxygen consumption during exercise (VO2max).

Results: Resting sPAP values were higher and FEV1, FVC and FEV1/FVC values were lower among smokers. As compared to resting values; FEV1 and FEV1/FVC ratio in smokers decreased significantly at peak exercise level (2.66±0.54 vs 2.35±0.49, p<0.01 and 81.57±8.21 vs 75.11±8.12, p<0.01 respectively). The HRRI values of all 1st, 2nd and 3rd minutes were significantly lower in the smoker group. Similar results were observed with CI and VO2max values (0.67±0.21 vs 0.76±0.19, p<0.01 and 34.91±4.63 vs 38.47±3.24, p<0.01 respectively). In addition, all mentioned parameters were significantly correlated with smoking duration.

Conclusion: Smoking is associated with a variety of adverse effects that may eventually reduce the exercise capacity of healthy individuals. These effects can manifest at early stages, and their severity correlates significantly with smoking duration.

Keywords: Smoking, physical exercise, cardiopulmonary function, chronotropic incompetence

INTRODUCTION

Smoking is a major preventable cause of morbidity and mortality worldwide due to its association with numerous pulmonary and cardiovascular diseases as well as cancer.[1] The airway obstruction and inflammatory changes of chronic obstructive lung diseases are attributed to smoking.[2] On the other hand, smoking is a well-known modifiable risk factor for atherosclerosis and cardiovascular diseases.[3]

During exercise, the body's oxygen consumption increases. In response, the cardiopulmonary system goes through physiological changes or modulation mechanisms, such as increasing cardiac output via chronotropic responses and enhancing the respiratory system's ventilatory capacity to meet body demands.[4,5] Smoking has been shown to have adverse effects on cardiac autonomic responses to exercise specifically in relation to the chronotropic responses and heart rate recovery (HRR).[6,7] The evaluation of these parameters can give an insight on cardiac modulation mechanisms during physical exercise.[8,9] Studies have also demonstrated that smoking is correlated with a decline in lung function, which consequently leads to potential limitations on an individual's daily activities and exercise capacity.[10] The evaluation of pulmonary function can be achieved using a spirometer. Furthermore, the assessment of maximal oxygen uptake (VO2max) during physical activity can provide valuable insights on individual's aerobic endurance performance. 11 In addition, smoking may also increase the pulmonary arterial pressure because of chronic hypoxia, increased pulmonary angiotensin-converting enzyme activity and increased sympathetic activation leading to chronic vasoconstriction of the pulmonary arteries.[12,13] Typically, systolic pulmonary artery pressure (sPAB) rises linearly with cardiac output;

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however, An abnormal increase in sPAB can be an early indicator of pulmonary vascular disease, which can eventually disrupt exercise capacity and respiratory health.[14]

Impaired or decreased physical activity during the middle age years can increase the risk of premature death and impede healthy aging.[15] The aim of our study was to assess the impact of smoking and its duration on diverse cardiopulmonary modulation mechanisms during physical exercise among middle-aged non-obese healthy individuals in order to provide a comprehensive understanding of the implications of smoking on physical fitness and exercise capacity.

METHODS

The study was carried out with the permission of Lokman Hekim University Scientific Researches Ethics Committee (Date: 21.12.2022, Decision No: 2022/196). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population and Design

This retrospective study evaluated middle-aged healthy individuals who presented to our cardiology outpatient clinic between June and December 2022. Individuals with a body mass index (BMI) exceeding 30 kg/m² were not subjected to evaluation. The smoking status and the duration of smoking were documented. Fasting blood glucose, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, and hemoglobin levels with kidney, liver, and thyroid function test results were taken from recent medical records. The demographic data of all participants was also recorded. The exclusion criteria comprised the presence of any cardiovascular, pulmonary, or other systemic diseases like hypertension or diabetes. Participants with impaired liver, renal, and thyroid function tests or electrolyte disturbances were also excluded. Consequently, a total of 243 individuals, comprising 142 smokers and 101 non-smokers, were included in the study.

Transthoracic echocardiography (TTE)

All subjects underwent two-dimensional echocardiography examination using Philips Epiq 5 device. Continuous wave (CW) Doppler of the tricuspid valve regurgitation (TR) tracing was used to measure the pressure difference between the right ventricle and the right atrium. In the simplified Bernoulli formula (P=4 [TRmax]2), the value obtained by the CW replacing over TR and the pressure difference between the right atrium and ventricle was calculated. The value obtained from the Bernoulli formula is calculated by the addition of right atrial pressure (RAP) to calculate sPAP.[16,17]

Respiratory Function Test (RFT)

The test was performed using a digital spirometer (SP10, Contec Medical, China). After deep inspiration, the subjects were asked to perform a vigorous expiration to the spirometer. The same procedure was performed three times successively. Measurements of Forced vital capacity (FVC), forced expiratory volume in the first second (FEV1) and FEV1/FVC ratio we recorded. The obtained vales from three different measurements were determined using averages. Subjects with FEV1/FVC ratio less than 70% were considered to have obstructive findings and were excluded.

Pulse Oximetry

Peripheral oxygen saturation (POS) of study participants was measured by pulse oximetry. The measurements were taken in normal room temperature. During a one-minute pulse oximetry measurement, the most frequently repeated value was recorded.

Treadmill Exercise Test (TET)

All the participants performed the TET. Before starting the test, basal sPAP, RFT, and POS values were recorded. Participants abstained from heavy eating, coffee and alcohol, and smokers from smoking two days before the test day. Drugs that are likely to influence the reliability of the test were discontinued. Blood pressure and 12-lead ECG recordings were obtained every 3 min over the course of stress testing and in the 1st, 2nd and 3rd minutes of recovery. HRRI values were obtained by subtracting the first, second, and third-minute recovery HR values from the peak HR value. Measurements of sPAP, POS, and RFT were repeated during peak exercise and after the 3rd minute of the recovery period. The chronotropic index was calculated using the formula; (Maximal HR - Resting HR)/(Predicted maximal HR - Resting HR).18 The VO2 max was calculated using the formula (Males: 3.88 + 0.056 × D and Females: 1.06 + 0.056 × D, where D= test duration in seconds).11

Statistical Analysis

The normal distribution of continuous variables was assessed using the Kolmogorov-Smirnov test and were defined as means±standard deviation. Categorical variables are commonly presented using percentages and frequencies. The Student's t-test was used to assess the differences between continuous variables, while the Chi-square test was utilized to examine associations among categorical variables. The paired samples T-test was used to compare the different values within the same group. Z test was used to compare ratios. Pearson correlation test was used to determine the correlation between the variables. P <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 24.0 (IBM Co., USA).

RESULTS

The baseline clinical features and socio-demographic characteristics showed no statistically significant differences between the study groups (Table 1). The mean smoking duration was 17.13±8.63 year. Resting sPAP values were significantly higher and the FEV1, FVC, FEV1/FVC and POS values were significantly lower in the smoker group. There was no difference between the study groups in terms of resting and peak exercise HR, but the 1st, 2nd, and 3rd minute-recovery HR were significantly higher in the smoker group. The HRRI in the smoker group was significantly lower than the non-smokers in all of 1st, 2nd and the 3rd minutes. The CI and VO2max values were significantly lower in the smoker group (Table 2). The sPAP values of the smoker group were significantly higher on peak exercise and during the recovery period. Contrarily, the peak and recovery values of all FEV1, FVC, FEV1/FVC and POS were significantly lower in the smoker group (Table 2).

AS compared to resting values, both FEV1 and FEV1/FVC ratio decreased significantly at the peak exercise level of the smoker group (2.66±0.54 vs 2.35±0.49, p<0.01 and 81.57±8.21 vs 75.11±8.12, p<0.01, respectively). This decline in respiratory function was not significant in the non-smoker group (2.84±0.49 vs 2.74±0.71, p=0.25 and 83.64±5.35 vs 82.31±2.04, p=0.21 respectively). Regarding sPAP values, there was a significant increase in sPAP values during peak exercise as compared to resting values in the smoker group (34.67±5.42 vs 44.69±7.47, p<0.01), this increase was less significant among controls (18.95±3.35 vs 20.12±3.91, p=0.023).

Table 1. Socio-demographic characteristics and baseline clinical features of study participants

Variables	Smoker Group (n=142)	Control group (n=101)	P value
Age, years	43.72±11.53	41.27±9.53	0.69
Gender			
Male, %	70.62	70.29	0,96
Female, %	29.38	29.71	0,96
BMI, kg/m²	25.35±2.73	25.52±2.91	0,64
Basal SBP, mm Hg	124.73±13.52	123.27±12.81	0,39
Basal DBP, mm Hg	74.83±8.16	75.10±7.94	0,79
Total Cholesterol, mg/dl	169.27±40.63	170.05±35.72	0,87
LDL, mg/dl	107.63±21.94	106.91±19.62	0,79
Triglycerides, mg/dl	161.63±21.73	160.95±20.83	0,8
Hemoglobin, gr/dl	14.36±2.93	14.44±2.85	0,83
Calcium, mg/dl	9.83±1.25	9.81±0.99	0,89
Sodium, mEq/L	140.94±2.94	141.07±1.89	0,69
Potassium, mEq/L	4.07±0.63	4.11±0.83	0,66
Magnesium, mg/dl	1.89±0.31	1.91±0.35	0,63

Abbr: BMI; Body Mass Index, SBP; Systolic Blood Pressure, DBP; Diastolic Blood Pressure, HR; Heart Rate, LV; Left Ventricle

Table 2. Comparison of the cardiopulmonary parameters of study participants during various levels of the treadmill exercise test

Variables	Smoker group (n=142)	Control group (n=101)	P value
On rest			
Resting HR	94.62±14.42	94.54±5.82	0.95
Resting sPAP	34.67±5.42	18.95±3.35	<0.01
Resting FEV1	2.66±0.54	2.84±0.49	0.01
Resting FVC	3.24±0.61	3.46±0.69	<0.01
Resting FEV1/FVC	81.57±8.21	83.64±5.35	0.027
Resting POS	96.01±1.72	96.59±1.24	<0.01
During peak exercise			
Peak HR	165.72±7.19	165.15±7.51	0.54
Chronotropic index	0.67±0.21	0.76±0.19	<0.01
VO2 Max	34.91±4.63	38.47±3.24	<0.01
Peak sPAP	44.69±7.47	20.12±3.91	<0.01
Peak FEV1	2.35±0.49	2.74±0.71	<0.01
Peak FVC	3.19±0.57	3.39±0.61	<0.01
Peak FEV1/FVC	75.11±8.12	82.31±2.04	<0.01
Peak POS	91.90±0.97	96.18±0.98	<0.01
During the recovery period			
1st minute Recovery HR	135.13±14.59	130.98±7.62	<0.01
2nd minute Recovery HR	118.37±14.51	111.16±6.54	<0.01
3rd minute Recovery HR	111.69±16.68	95.05±8.89	<0.01
HRRI 1st minute	30.58±11.71	34.16±8.24	<0.01
HRRI 2nd minute	47.34±13.38	53.98±7.74	<0.01
HRRI 3rd minute	54.02±17.16	70.09±10.69	<0.01
Recovery sPAP	39.37±7.36	17.19±2.27	<0.01
Recovery FEV1	2.51±0.57	2.77±0.47	<0.01
Recovery FVC	3.21±0.69	3.44±0.62	<0.01
Recovery FEV1/FVC	79.25±8.52	84.29±2.21	<0.01
Recovery POS	94.20±1.55	97.22±0.86	<0.01

Abbr: HR; Heart Rate, sPAP; systolic pulmonary artery pressure, FEV1; forced expiratory volume during the 1st second, FVC; forced vital capacity, POS; partial oxygen saturation, HRRI; heart rate recovery index

In the smoker group, there was a statistically significant negative correlation between smoking duration and the HRRI values. A significant negative correlation was also observed between smoking duration and the CI, VO2max, resting FEV1, resting FVC, resting FEV1/FVC, and resting POS values. In addition, there was a statistically significant positive correlation between smoking duration and resting sPAP values (Table 3).

Table 3. The correlations between smoking duration and parameters of cardiopulmonary function

Variables	Correlation with smoking duration	
	R-value	P-value
HRRI 1	-0.78	<0.01
HRRI 2	-0.64	<0.01
HRRI 3	-0.51	<0.01
VO2 Max	-0.38	<0.01
Chronotropic index	-0.43	<0.01
Resting sPAP	0.64	<0.01
Resting FEV1	-0.48	<0.01
Resting FVC	-0,36	<0.01
Resting FEV1/FVC	-0.41	<0.01
Resting POS	-0.38	<0.01

Abbr: HR; Heart Rate, sPAP; systolic pulmonary artery pressure, FEV1; forced expiratory volume during the 1st second, FVC; forced vital capacity, POS; partial oxygen saturation, HRRI; heart rate recovery index

DISCUSSION

The present study assessed the overall effects of smoking on the cardiopulmonary modulation mechanisms during physical exercise in middle-aged non-obese healthy individuals. Study results demonstrated that during physical exercise smokers exhibited a more significant decline in respiratory function parameters, including FEV1, FVC and FEV1/FVC with lower VO2max and POS levels, as compared to non-smokers. Furthermore, a more exagurated increase in sPAB was seen among smokers. On the other hand, the autonomic responses to exercise as evaluated by the CI and HRRI were lower in the smoker group. These variations were in correlation with smoking duration.

The effects of smoking on the pulmonary system can be attributed to a variety of factors. It promotes the destruction of alveolar walls and the expansion of air spaces distal to the terminal bronchioles, resulting in airway obstruction and diminished lung function.[2] Smoking is also known to cause fatigue of the skeletal muscles, and studies have concluded that abnormalities in skeletal muscles endurance can result in abnormalities of breathing efficiency.[19,20] Both airflow obstruction and breathing abnormalities may lead to hyperinflation and decreased exercise capacity. These consequences can be seen even in the early phases of cigarette smoking.[21] Twisk et al. reported that smoking deteriorates lung function by causing a decrease in the FVC and FEV1.[22] Another more recent study showed that smoking is associated with a significant decrease in FEV1/FVC ratio.[23] Similar findings were observed in the spirometry results of our study participants at rest. Furthermore, smoking duration was significantly correlated with all of FEV1, FVC and FEV1/FVC values at rest. While both groups experienced a decline in these parameters during peak exercise and the recovery period, study results showed that the decline in FEV1 and FEV1/FVC ratio is more significant among smokers. These findings suggests that in addition to the chronic obstructive effects of smoking on respiratory airways during rest, it can cause further deterioration of respiration during exercise, and continue even in the period of recovery. In our study, oxygen saturation levels were also measured on rest, during peak exercise and in the recovery period and similar results were observed.

Other than the pulmonary system, effects of smoking on the autonomous nervous system have been studied for a long time. Studies showed that smoking impairs the sympathetic activation and vagal modulation of the heart during exercise.[24] The increased metabolic demands during exercise are met by increasing cardiac output, which is accomplished by an increase in heart rate and stroke volume. This increase in HR is regulated by exercise induced autonomic control, where sympathetic activity increases, and vagal tone is reduced.[25] Smokers may experience chronotropic incompetence, which encounter a diminished HR response to exercise and considered as a predictor of cardiovascular mortality.[11] The smoker participants of our study had lower values of CI than non-smokers, which supports the association of smoking with chronotropic incompetence even in healthy individuals.

After the termination of exercise, sympathetic activity is withdrawn, and vagal reactivation causes the heart rate to return to baseline levels. The activation of the parasympathetic nervous system is significant in the early period after exercise, whereas the withdrawal of the sympathetic nervous system is effective in the later period.[26] Evaluating HRRI gives an idea about the parasympathetic response of the autonomic nervous system to exercise and its association with cardiovascular diseases.[27] In parallel to this, we observed a significant decrease in the HRRI rates of the 1st, 2nd, and 3rd minutes for smokers compared to nonsmokers. Since our study population is composed of healthy individuals, we can conclude that the effect of smoking on HRRI is independent from other comorbidities and that smoking can directly be responsible of exaggerating the sympathetic activity and suppressing the vagal response during physical exercise. Moreover, the parameters of autonomic modulation during exercise were all significantly correlated with smoking duration.

Another more recent predictor of cardiopulmonary function during exercise is VO2max. Studies showed that the evaluation of VO2max can be used to quantify endurance fitness and exercise capacity.[28] The smoker participants of our study had significantly lower VO2max values than non-smokers, implying a decline in physical fitness as a result of smoking. The changes in VO2max were also correlated with smoking duration.

In addition to the previous studies, we also examined the effects of smoking on the pulmonary circulation during exercise and the recovery period. Smoking is known to cause pulmonary artery remodeling and hypoxic vasoconstriction, both of which may contribute to the development of pulmonary hypertension (PH).[29] In our study, we measured the sPAP of study participants at rest and compared it to sPAP measurements taken during the peak exercise and the recovery period. At rest, sPAP values were significantly higher among smokers and resting sPAP values were correlated with smoking duration. Furthermore, smokers had significantly higher peak exercise and recovery sPAP values compared to baseline levels. Whereas the increase of sPAP in the non-smoker group was less significant. Beside the chronic morphological changes of the pulmonary vasculature,

the increased sympathetic activity seen among the smoker participants of our study may be the reason of the higher increase and the delayed fall of sPAP during exercise.[30]

The main limitation of our study was the small sample size; with a larger population, more precise data could be obtained. Moreover, the absence of randomization in the design constituted an important limitation. The impact of daily lifestyle habits, including dietary patterns, alcohol consumption, and the routine daily activity, on exercise performance was not assessed. In addition, smoking status was determined based on patients' self-reports rather than a more reliable test, such as the exhaled carbon monoxide or serum nicotine tests, which were unavailable.

CONCLUSION

Our study demonstrated that smoking is associated with a number of negative consequences that may eventually limit exercise capacity and have an adverse effect on healthy aging. These deleterious effects may start at early stage of smoking but are significantly correlated with smoking duration.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Lokman Hekim University Scientific Researches Ethics Committee (Date: 21.12.2022, Decision No: 2022/196).

Informed Consent: Because the study was designed retrospectively, no written informed consent from was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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